CLAIMS

We claim:

1. A compound of the following formula:

$$R^{1}$$
— X — $(CH_{2})_{n}$
 A
 A
 B
 $CO_{2}R^{3}$

Formula I

wherein:

n is 0, 1 or 2;

X is CH₂, C=O, O, S or NH;

A is a natural or unnatural amino acid of Formula IIa-i:

$$R^9$$
 $(CH_2)_a$
 $(CH_2)_b$
 $(CH_2)_b$

B is a hydrogen atom, a deuterium atom, C₁₋₁₀ straight chain or branched alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, 2-benzoxazolyl, substituted 2-oxazolyl, (CH₂)_mcycloalkyl, (CH₂)_mphenyl, (CH₂)_m(substituted phenyl), (CH₂)_m(1 or 2-naphthyl), (CH₂)_mheteroaryl, halomethyl, CO₂R¹³, CONR¹⁴R¹⁵, CH₂ZR¹⁶, CH₂OCO(aryl), CH₂OCO(heteroaryl), or CH₂OPO(R¹⁷)R¹⁸, where Z is an oxygen or a sulfur atom, or B is a group of the Formula IIIa-c:

R¹ is phenyl, substituted phenyl, naphthyl, substituted naphthyl, heteroaryl, or substituted heteroaryl;

 R^2 is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, $(CH_2)_mNH_2$, $(CH_2)_mNHCOR^{10}$, $(CH_2)_mN(C=NH)NH_2$, $(CH_2)_pCO_2R^3$, $(CH_2)_pOR^{11}$, $(CH_2)_pSR^{12}$, $(CH_2)_mcycloalkyl$, $(CH_2)_mphenyl$, $(CH_2)_m(substituted phenyl)$, $(CH_2)_m(1$ or 2-naphthyl), or $(CH_2)_m$ heteroaryl, wherein heteroaryl includes (but is not limited to)

pyridyl, thienyl, furyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazinyl, pyrimidyl, triazinyl, tetrazolyl, and indolyl;

R³ is hydrogen, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or substituted phenylalkyl;

and wherein

 R^4 is alkyl, cycloalkyl, phenyl, substituted phenyl, $(CH_2)_mNH_2$, $(CH_2)_mNHCOR^{10}$, $(CH_2)_mN(C=NH)NH_2$, $(CH_2)_pCO_2R^3$, $(CH_2)_pOR^{11}$, $(CH_2)_pSR^{12}$, $(CH_2)_mcycloalkyl$, $(CH_2)_mphenyl$, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m(1$ or 2-naphthyl), or $(CH_2)_m$ heteroaryl, wherein heteroaryl includes (but is not limited to) pyridyl, thienyl, furyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazinyl, pyrimidyl, triazinyl, tetrazolyl, and indolyl;

 R^{4a} is hydrogen, or methyl, or R^4 and R^{4a} taken together are $-(CH_2)_d$ - where d is an interger from 2 to 6;

R⁵ is phenyl, substituted phenyl, (CH₂)_pphenyl, (CH₂)_p(substituted phenyl), cycloalkyl, or benzofused cycloalkyl;

 R^6 is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

 R^7 is hydrogen, fluorine, oxo, alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m$ (1 or 2-naphthyl), OR^{11} , SR^{12} , or NHCOR¹⁰;

 R^8 is hydrogen, oxo, alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

 R^9 is alkyl, cycloalkyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m$ (1 or 2-naphthyl), or COR^{10} ;

 R^{10} is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m$ (1 or 2-naphthyl), OR^{13} , or $NR^{14}R^{15}$;

 R^{11} is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

 R^{12} is alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

 R^{13} is alkyl, cycloalkyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

 R^{14} is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, $(CH_2)_m$ cycloalkyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), or $(CH_2)_m$ (1 or 2-naphthyl);

R¹⁵ is hydrogen or alkyl; or

R¹⁴ and R¹⁵ taken together form a five, six or seven membered carbocyclic or heterocyclic ring, such as morpholine or N-substituted piperazine;

 R^{16} is phenyl, substituted phenyl, naphthyl, substituted naphthyl, heteroaryl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m$ (1 or 2-naphthyl), or $(CH_2)_m$ heteroaryl;

R¹⁷ and R¹⁸ are independently alkyl, cycloalkyl, phenyl, substituted phenyl, naphthyl, or phenylalkyl, substituted phenylalkyl, or (cycloalkyl)alkyl;

 R^{19} and R^{20} are independently hydrogen, alkyl, phenyl, substituted phenyl, $(CH_2)_m$ phenyl, or $(CH_2)_m$ (substituted phenyl), or R^{19} and R^{20} taken together are -(CH=CH)₂-;

 R^{21} is hydrogen, alkyl, phenyl, substituted phenyl, $(CH_2)_m$ phenyl, $(CH_2)_m$ (substituted phenyl);

R²², R²³ and R²⁴ are independently hydrogen or alkyl;

Y¹ is CH₂, (CH₂)₂, (CH₂)₃, or S;

 Y^2 is O or NR^{24} ;

 Y^3 is CH_2 , O, or NR^{24} ;

a is 0 or 1 and b is 1 or 2, provided that when a is 1 then b is 1;

c is 1 or 2, provided that when c is 1 then a is 0 and b is 1;

m is 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

- 2. The compound of claim 1 where X is oxygen.
- 3. The compound of claim 1 where X is sulfur.
- 4. The compound of claim 1 where X is NH.
- 5. The compound of claim 1 where X is CH_2 .
- 6. The compound of claim 1 where X is C=0.

7. The compound of claim 1 wherein A is

$$\begin{array}{c|c}
 & R^4 \\
 & R^{4a} \\
 & O
\end{array}$$
IIa

8. The compound of claim 7 wherein

 R^4 is lower alkyl, cycloalkyl, phenyl, substituted phenyl, $(CH_2)_nNH_2$, $(CH_2)_mOR^{10}$, $(CH_2)_mSR^{11}$, $(CH_2)_ncycloalkyl$, $(CH_2)_nphenyl$, $(CH_2)_n(substituted phenyl)$, or $(CH_2)_n(1 \text{ or } 2\text{-naphthyl})$; and

R^{4a} is hydrogen.

9. The compound of claim 1 wherein A is

10. The compound of claim 9 wherein R⁵ is phenyl, substituted phenyl, (CH₂)_mphenyl, (CH₂)_m(substituted phenyl), cycloalkyl, or 2-indanyl.

11. The compound of claim 1 wherein A is

- 12. The compound of claim 11 wherein R^7 is hydrogen, fluorine, cycloalkyl, phenyl, substituted phenyl, naphthyl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ phenyl, $(CH_2)_n$ (substituted phenyl), $(CH_2)_n$ (1 or 2-naphthyl), $(CH_3)_n$ 0, or $(CH_3)_n$ 1.
 - 13. The compound of claim 1 wherein A is

14. The compound of claim 13 wherein

 R^8 is hydrogen, oxo, cycloalkyl, phenyl, substituted phenyl, or naphthyl; and

 Y^1 is CH_2 , $(CH_2)_2$, $(CH_2)_3$, or S.

15. The compound of claim 1 wherein A is

$$(CH_2)_a$$
 $(CH_2)_b$
 O
IIh

- 16. The compound of claim 15 wherein a is 0.
- 17. The compound of claim 1 wherein

B is hydrogen, 2-benzoxazolyl, substituted 2-oxazolyl, CH_2ZR^{15} , $CH_2OCO(aryl)$, or $CH_2OPO(R^{16})R^{17}$; and

Z is O or S.

18. The compound of claim 1 wherein B is

- 19. The compound of claim 18 wherein R^{19} and R^{20} are independently hydrogen, alkyl, or phenyl, or wherein R^{19} and R^{20} taken together are -(CH=CH)₂-.
 - 20. The compound of claim 1 wherein

X is O or NH;

n is 0 or 1;

R1 is substituted phenyl, naphthyl, or substituted naphthyl;

 R^2 is hydrogen, lower alkyl, $(CH_2)_pCO_2R^3$, $(CH_2)_m$ (substituted phenyl), $(CH_2)_m$ (1- or 2-naphthyl), or $(CH_2)_m$ tetrazolyl; and

R³ is hydrogen or lower alkyl.

- 21. The compound of claim 20 wherein R¹ is 1-naphthyl.
- 22. The compound of claim 20 wherein R¹ is 2-naphthyl.
- 23. The compound of claim 20 wherein R¹ is substituted naphthyl.
- 24. The compound of claim 23 wherein substituted naphthyl is 2-carboxy-1-naphthyl.
 - 25. The compound of claim 20 wherein R¹ is substituted phenyl.
- 26. The compound of claim 25 wherein substituted phenyl is 2-substituted phenyl.

- 27. The compound of claim 26 wherein 2-substituted phenyl is (2-phenyl)phenyl.
- 28. The compound of claim 20 wherein A is alanine, valine, leucine cyclohexylalanine, phenylgycine or t-butylglycine.
 - 29. The compound of claim 28 wherein R¹ is 1-naphthyl.
 - 30. The compound of claim 28 wherein R^1 is 2-naphthyl.
 - 31. The compound of claim 28 wherein R¹ is substituted naphthyl.
- 32. The compound of claim 31 wherein substituted naphthyl is 2-carboxy-1-naphthyl.
 - 33. The compound of claim 28 wherein R^1 is 2-substituted phenyl.
- 34. The compound of claim 33 wherein 2-substituted phenyl is (2-phenyl)phenyl.
- 35. The compound of claim 20 wherein R^2 is $(CH_2)_2CO_2R^3$ and n is 0.
- 36. A pharmaceutical composition comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

- 37. A method for treating an autoimmune disease, comprising administering an effective amount of the pharmaceutical composition of claim 36 to a patient in need thereof.
- 38. A method of treating an inflammatory disease, comprising administering an effective amount of the pharmaceutical composition of claim 36 to a patient in need thereof.
- 39. A method of treating a neurodegenerative disease, comprising administering an effective amount of the pharmaceutical composition of claim 36 to a patient in need thereof.
- 40. A method of preventing ischemic injury to a patient suffering from a disease associated with ischemic injury, comprising administering an effective amount of the pharmaceutical composition of claim 36 to a patient in need thereof.
- 41. A method for expanding of hematopoietic cell populations or enhancing their survival, comprising contacting the cells with an effective amount of the pharmaceutical composition of claim 36.
- 42. The method of claim 41 wherein the cell populations are granulocytes, monocytes, erthrocytes, lymphocytes or platelets for use in cell transfusions.
- 43. A method of prolonging the viability of an organ that has been removed from a donor or isolated cells derived from an organ for the purpose of a

future transplantation procedure, comprising applying an effective amount of the pharmaceutical composition of claim 36 to the organ or isolated cells to prolong the viability of the same as compared to untreated organ or isolated cells.

- 44. The method of claim 43 wherein the organ is an intact organ.
- 45. The method of claim 43 wherein the isolated cells are pancreatic islet cells, dopaminergic neurons, blood cells or hematopoietic cells.